



Attorney's Docket No. 035510/305985 (P-6186)

PATENT

In The United States Patent And Trademark Office

Appl. No.: 10/664,037
Applicant(s): Guarino et al.
Filed: September 17, 2003
Art Unit: 1651
Examiner: Vera Afremova
Title: ENVIRONMENTS THAT MAINTAIN FUNCTION OF
PRIMARY LIVER CELLS

Confirmation No.: 2610

Docket No.: 035510/305985 (P-6186)
Customer No.: 47656

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**APPEAL BRIEF TRANSMITTAL
(PATENT APPLICATION – 37 C.F.R. § 41.37)**

1. Transmitted herewith is the APPEAL BRIEF in this application, with respect to the Notice of Appeal filed on January 4, 2007.
2. ☐ Applicant claims small entity status.
3. Pursuant to 37 C.F.R. § 41.20(b)(2), the fee for filing the Appeal Brief is:
☐ small entity \$250.00
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Appeal Brief fee due \$500
☒ Fee is Enclosed
☐ Please charge the fee to Deposit Account 16-0605.
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Respectfully submitted,

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Registration No. 52,706

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APPEAL BRIEF UNDER 37 CFR § 41.37

This Appeal Brief is filed pursuant to the "Notice of Appeal to the Board of Patent Appeals and Interferences" filed January 4, 2007.

1. Real Party in Interest

The real party in interest in this appeal is Becton, Dickinson and Company, the assignee of the above-referenced patent application.

2. Related Appeals and Interferences

There are no related appeals and/or interferences involving this application or its subject matter.

3. Status of Claims

Claims 1-57 were filed with the original specification. Thereafter, claims 58-67 were added. Claims 4, 5 and 17-57 have been canceled. Claims 9, 11, 59, and 60 have been

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withdrawn. Claims 1-3, 6-8, 10, 12-16, 58, and 61-67 have been considered by the Examiner and are rejected. Claims 1-3, 6-8, 10, 12-16, 58, and 61-67 are the subject of this appeal.

4. Status of Amendments

No new amendments have been made to the claims.

5. Summary of Claimed Subject Matter

Independent claim 1 of the present application is drawn to a method for culturing primary liver cells. The method includes providing a polymer composition including a cell adhesion resistant (CAR) material, and one or more extracellular matrix (ECM) proteins and a polycationic polymer bound to the CAR material, where the CAR material, one or more ECM proteins and polycationic polymer form a cell adhesion promoting surface, and incubating the liver cells in the presence of the surface in a medium that supports growth and/or maintenance of the liver cells, such that the liver cells attach to the surface (see, *e.g.*, page 2, line 18 through page 3, line 11; page 4, lines 7-23; page 5, lines 3-8 and 13-25; page 11, lines 17-24; and page 12, lines 13-19).

Independent claim 58 of the present application is drawn to a method for culturing primary liver cells. The method includes providing a polymer composition including a CAR material, and collagen I and poly-L-ornithine bound to the CAR material, where the CAR material, collagen I and poly-L-ornithine form a cell adhesion promoting surface, and incubating the liver cells in the presence of the surface in a medium that supports growth and/or maintenance of the liver cells, such that the liver cells attach to the surface (see, *e.g.*, page 2, line 18 through page 3, line 11; page 4, lines 7-23; page 5, lines 3-8 and 13-25; page 8, lines 12-14; page 11, lines 17-24; and page 12, lines 13-19).

6. Grounds of Rejection to Be Reviewed on Appeal

Issue 1—Whether claims 1-4, 7, 8, 12-15, and 62-64 are anticipated by published International Application WO 98/56897 (the '897 application) under 35 U.S.C. § 102(b).

Issue 2—Whether claims 1-3, 7, 8, 14-16, and 62-64 are anticipated by U.S. Patent No. 6,562,616 (the ‘616 patent) under 35 U.S.C. § 102(e).

Issue 3—Whether claims 1-3, 7, 8, 14, 15, and 61-64 are anticipated by U.S. Patent No. 5,942,436 (the ‘436 patent) under 35 U.S.C. § 102(b).

Issue 4—Whether claims 1-3, 6-8, 10, 12-16, 58, and 61-67 are obvious in light of the ‘897 application, the ‘616 patent and the ‘436 patent in view of U.S. Patent No. 6,653,105 (the ‘105 patent) and published Japanese Application JP 04322657 (the ‘657 application) under 35 U.S.C. § 103(a).

7. **Argument**

(a) Grouping of Claims

Appellants believe that the claims do not stand or fall together. The rejected claims are all drawn to methods for culturing primary liver cells. However, the claims differ from each other in the substances bound to the CAR material. That is, independent claim 1 and dependent claims 2, 3, 6-8, 12-16, and 61-64 require that one or more ECM proteins and a polycationic polymer be bound to the CAR material, while dependent claim 10, independent claim 58 and dependent claims 65-67 contain limitations requiring that collagen I and poly-L-ornithine be bound to the CAR material. While Appellants believe that all these claims are allowable, it is conceivable that among claims with differing requirements for the substances bound to the CAR material, some claims could be found novel and non-obvious while others might not. Therefore, the method claims do not all stand or fall together.

(b) Issue 1—Whether claims 1-4, 7, 8, 12-15, and 62-64 are anticipated by the ‘897 application under 35 U.S.C. § 102(b).

The Examiner has rejected claims 1-4, 7, 8, 12-15, and 62-64 under 35 U.S.C. § 102(b) as allegedly being anticipated by the ‘897 application. Specifically, the Examiner asserts that the ‘897 application discloses a method for culturing primary porcine liver cells by incubating the cells in plastic 24-well dishes including culture medium, HYAFF matrices (esters of hyaluronic acid with benzyl alcohol) and dermal fibroblasts (which provide ECM proteins). The Examiner

states that “[p]lastic is a polymer or a generic polycationic polymer within the broadest meaning of the claim. The liver cells are maintained alive for several weeks ... [t]hus, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed invention” (Office Action dated October 4, 2006, page 3, lines 10-15). For the following reason, the Examiner’s reasoning is not well founded.

I. The Examiner Has Made a Factual Error in This Rejection

Plastic is **not** a generic polycationic polymer within the broadest meaning of claims 1-4, 7, 8, 12-15, and 62-64. As is well known to one of ordinary skill in the art, polystyrene (the plastic generally employed in manufacturing plastic culture vessels) is a very hydrophobic (*i.e.*, nonwetable) polymer to which cells have difficulty attaching. Accordingly, standard polystyrene culture vessels are surface modified in an ionized atmosphere (*e.g.*, via corona discharge or gas-plasma) with highly energetic oxygen atoms which graft onto the surface polystyrene chains, such that the surface becomes hydrophilic and **negatively charged**.

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently (see, *e.g.*, *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)). Claims 1-4, 7, 8, 12-15, and 62-64 recite “providing a polymer composition comprising a CAR material, and one or more ECM proteins and a **polycationic** polymer bound to said CAR material, wherein said CAR material, said one or more ECM proteins, and said **polycationic** polymer thereby form a cell adhesion promoting surface.” Thus, these claims clearly require a **positively charged** polymer component of the cell adhesion promoting surface. Plastic does not provide such a **positively charged** polymer component.

As at least one limitation of claims 1-4, 7, 8, 12-15, and 62-64 is not expressly or inherently disclosed by the ‘897 application, the ‘897 application cannot anticipate these claims. Therefore, Appellants request that this rejection of claims 1-4, 7, 8, 12-15, and 62-64 be overturned.

(c) Issue 2—Whether claims 1-3, 7, 8, 14-16, and 62-64 are anticipated by the ‘616 patent under 35 U.S.C. § 102(e).

The Examiner has rejected claims 1-3, 7, 8, 14-16, and 62-64 under 35 U.S.C. § 102(e) as allegedly being anticipated by the ‘616 patent. Specifically, the Examiner asserts that the ‘616 patent discloses a method for culturing primary porcine liver cells by incubating the cells on collagen type I coated glass slides. The Examiner states that the ‘616 patent “also teaches the use of a polycationic polymer or PDMS polymer materials for forming surface composition in the method for culturing liver cells. The liver cells are maintained in viable state ... [t]herefore, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed invention” (Office Action, page 4, lines 10-15). For the following reasons, the Examiner’s reasoning is not well founded.

I. The ‘616 Patent Does Not Teach The Use of Polycationic Polymer Materials For Forming a Surface Composition

Contrary to the Examiner’s assertion, the ‘616 patent does not teach the use of polycationic polymer materials for forming a surface composition in the disclosed method for culturing liver cells. Rather, the ‘616 patent discloses a two-compartment, parallel-plate bioreactor with an internal membrane oxygenator in which hepatocytes cultured on glass slides coated with type I collagen are maintained (column 24, lines 52-54 and column 25, lines 16-30 and 55-57).

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently (see, *e.g.*, *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)). Claims 1-3, 7, 8, 14-16, and 62-64 recite “providing a polymer composition comprising a CAR material, and one or more ECM proteins and a polycationic polymer bound to said CAR material, wherein said CAR material, said one or more ECM proteins, and said polycationic polymer thereby form a cell adhesion promoting surface.” While the ‘616 patent does disclose culturing hepatocytes on glass slides coated with

type I collagen (an ECM protein), it does not expressly or inherently teach a polycationic polymer component of the cell adhesion promoting surface.

II. The Examiner Has Made a Factual Error in This Rejection

As described above, the Examiner alleges that the '616 patent teaches the use of PDMS (polydimethylsiloxane) polymer material for forming a surface composition in the disclosed method for culturing liver cells. Appellants respectfully disagree with this assertion.

As an initial matter, PDMS is not a **polycationic** polymer, but rather a polymer composed of repeating $\text{SiO}(\text{CH}_3)_2$ monomers. Furthermore, as described in the '616 patent, custom molded PDMS seeding chambers were used to allow "for collagen coating and seeding of the slide with hepatocytes without spillage over the edges of the slide" (column 24, line 67 through column 25, line 3). Thus, the PDMS material formed a seeding chamber in which collagen-coated slides were placed, rather than forming part of the surface composition upon which the hepatocytes were cultured.

Because the '616 patent does not expressly or inherently teach all of the elements of claims 1-3, 7, 8, 14-16, and 62-64, the '616 patent cannot anticipate these claims. Therefore, Appellants request that this rejection of claims 1-3, 7, 8, 14-16, and 62-64 be overturned.

(d) Issue 3—Whether claims 1-3, 7, 8, 14, 15, and 61-64 are anticipated by the '436 patent under 35 U.S.C. § 102(b).

The Examiner has rejected claims 1-3, 7, 8, 14, 15, and 61-64 under 35 U.S.C. § 102(b) as allegedly being anticipated by the '436 patent. Specifically, the Examiner asserts that the '436 patent discloses a method for culturing primary liver cells such as rat hepatocytes and human hepatocytes in culture vessels coated with type I collagen. The Examiner states that "[p]lastic is polymer that is a generic CAR material and a generic polycationic polymer within the broadest meaning of the claims. The patent teaches that liver cells are maintained in functional state ... [t]hus, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed

invention” (Office Action, page 5, lines 10-17). For the following reason, the Examiner’s reasoning is not well founded.

I. The Examiner Has Made a Factual Error in This Rejection

As discussed in detail above, plastic is **not** a generic polycationic polymer within the broadest meaning of claims 1-3, 7, 8, 14, 15, and 61-64.

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently (see, *e.g.*, *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)). Claims 1-3, 7, 8, 14, 15, and 61-64 recite “providing a polymer composition comprising a CAR material, and one or more ECM proteins and a **polycationic** polymer bound to said CAR material, wherein said CAR material, said one or more ECM proteins, and said **polycationic** polymer thereby form a cell adhesion promoting surface.” Thus, these claims clearly require a **positively charged** polymer component of the cell adhesion promoting surface. Plastic does not provide such a **positively charged** polymer component.

As at least one limitation of claims 1-3, 7, 8, 14, 15, and 61-64 is not expressly or inherently disclosed by the ‘436 patent, the ‘436 patent cannot anticipate these claims. Therefore, Appellants request that this rejection of claims 1-3, 7, 8, 14, 15, and 61-64 be overturned.

(e) Issue 4—Whether claims 1-3, 6-8, 10, 12-16, 58, and 61-67 are obvious in light of the ‘897 application, the ‘616 patent and the ‘436 patent in view of the ‘105 patent and the ‘657 application under 35 U.S.C. § 103(a).

The Examiner has rejected claims 1-3, 6-8, 10, 12-16, 58, and 61-67 under 35 U.S.C. § 103(a) as allegedly being obvious in light of the ‘897 application, the ‘616 patent and the ‘436 patent in view of the ‘105 patent and the ‘657 application. This rejection is respectfully traversed.

The ‘105 patent teaches that polybasic amino acids, such as polyornithine and polylysine, and extracellular matrix proteins, such as laminin, collagen and fibronectin, can be used as

components of a surface coating composition for enhancing the growth of serum-free C3A cells. The clonally derived C3A cell line “retains most of the characteristics of the human hepatocyte parent C3A line” (column 4, lines 5-7). The ‘657 application teaches that a cell culture surface “on which many fine protrusions and groves are formed is brought into contact with cells or a tissue(s) selected from connective tissues and nerve, glia, Schwann, skin, muscle, kidney and liver cells” (English abstract). The ‘657 application further teaches that “one or a mixture of collagen, poly-L-lysine, poly-L-ornithine, laminin, fibronectin, [ch]ick plasma, artificial lipid films ... and nerve growth factors” can be adhered to the cell culture surface (English abstract).

As the Examiner has acknowledged, the ‘897 PCT, the ‘616 patent and the ‘436 patent are “lacking particular disclosure about the use of poly-L-ornithine in the surface coating composition in the method for culturing liver cells” (Office Action, page 6, lines 10-11). However, the Examiner contends that it “would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add poly-L-ornithine to the coating polymer compositions of [the ‘897 PCT, the ‘616 patent and/or the ‘436 patent] with a reasonable expectation of success in culturing liver cells because the cell attachment surfaces comprising poly-L-ornithine and collagen type I have been taught and/or suggested by the prior art of attaching, incubating and growing hepatocytes as adequately demonstrated by the cited reference combined” (Office Action, page 6, line 20 through page 7, line 3).

I. The Examiner’s Conclusion of Obviousness is Based on Improper Hindsight Reasoning

A claimed invention is unpatentable if the differences between it and the prior art are “such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.” *In re Kahn*, 441 F.3d 977, 985 (Fed. Cir. 2006) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 13-14 (1966)). “To reach a proper conclusion under §103, the decisionmaker must step backward in time and into the shoes worn by [a person having ordinary skill in the art] when the invention was unknown and just before it was made. In light of *all* the evidence, the decisionmaker must then determine whether . . . the

claimed invention as a whole would have been obvious at *that* time to *that* person” (emphasis in the original). *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Appellants submit that one of skill in the art **at the time the present invention was made** would not have been motivated to combine the teachings of the ‘897 application, the ‘616 patent and the ‘436 patent with the teachings of the ‘105 patent and the ‘657 application. As discussed above, the ‘105 patent teaches that polybasic amino acids, such as polyornithine and polylysine, and extracellular matrix proteins, such as laminin, collagen and fibronectin, can be used as components of a surface coating composition for enhancing the growth of serum-free C3A cells. Serum-free C3A cells (and the human hepatocyte parent C3A line from which the serum-free line is clonally derived) are not **primary liver cells** (*i.e.*, hepatocytes isolated directly from liver tissue), but rather an established human hepatocyte line. As is well known to one of ordinary skill in the art, the requirements for culturing primary liver cells are significantly different from those required for culturing an established hepatocyte line.

As also discussed above, the ‘657 application teaches that a cell culture surface having fine protrusions and groves and coated with one or a mixture of collagen, poly-L-lysine, poly-L-ornithine, laminin, fibronectin, chick plasma, artificial lipid films, and nerve growth factors, can be used to culture cells and tissues including connective tissues and nerve, glia, Schwann, skin, muscle, kidney and liver cells. However, general statements that one or a mixture of poly-L-ornithine, poly-L-lysine, laminin, collagen, fibronectin, chick plasma, artificial lipid films, and nerve growth factors may be used in culturing various cell types do not guide the skilled artisan in arriving at Appellants’ specific methods for culturing primary liver cells.

At best, the combined teachings of the ‘105 patent concerning culturing of serum-free C3A cells, and the disclosure of the ‘657 application that cells and tissues (including connective tissues and nerve, glia, Schwann, skin, muscle, kidney and liver cells) can be cultured on surfaces having fine protrusions and groves and coated with one or a mixture of a laundry list of substances, in combination with the teachings of the ‘897 application, the ‘616 patent and the ‘436 patent, merely invite experimentation. However, an invitation to experiment is not sufficient grounds to reject an invention as obvious. Where the prior art gives only general guidance as to the particular form of the invention or how to achieve it, as here, obviousness may

not be found. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81, 90-91 (Fed. Cir. 1986).

The mere fact that the different elements of an invention may be disclosed in the prior art is insufficient to establish obviousness without a motivation to combine the prior art references.

As noted by the Federal Circuit:

Most if not all inventions arise from a combination of old elements. Thus, every element of a claimed invention may often be found in the prior art. However, identification in the prior art of each individual part claimed is insufficient to defeat the patentability of the whole claimed invention. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. *In re Kotzab* 55 USPQ2d 1313, 1316 (Fed. Cir. 2000) (internal citations omitted).

In the present case, the cited references lack any suggestion or motivation to combine their teachings to arrive at the methods for culturing primary liver cells discovered by Appellants. Given the lack of evidence of a motivation to combine the references, it appears that the Examiner has engaged in impermissible "hindsight reconstruction" in formulating the present rejection. See *In re Fine*, 5 USPQ2d 1071, 1075 (Fed. Cir. 1988) (holding that "[o]ne cannot use hindsight reconstruction to pick and choose among disclosures in the prior art to deprecate the claimed invention"). In establishing obviousness, it is improper "to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992).

In view of the above arguments, Appellants contend that a *prima facie* case of obviousness under 35 U.S.C. § 103(a) has not been established. Therefore, Appellants request that this rejection of claims 1-3, 6-8, 10, 12-16, 58, and 61-67 be overturned.

II. Claims 10, 58 and 65-67 Should Be Considered Separately

Claims 10, 58 and 65-67 contain limitations requiring that collagen I and poly-L-ornithine be bound to the CAR material, where the CAR material, the collagen I and the poly-L-ornithine thereby form a cell adhesion promoting surface for culturing primary liver cells.

Appellants submit that claims 1-3, 6-8, 10, 12-16, 58, and 61-67 are novel and non-obvious over the '897 application, the '616 patent, the '436 patent, the '105 patent, and the '657 application for the reasons discussed above. However, should the Board disagree, claims requiring that collagen I and poly-L-ornithine be bound to the CAR material (*i.e.*, claims 10, 58 and 65-67) are narrower in scope and thus should be considered separately in view of the arguments presented above.

Specifically, the teachings of the '105 patent that polybasic amino acids and ECM proteins can be used to enhance growth of an established hepatocyte line, and of the '657 application that multiple cell and tissue types can be cultured on grooved surfaces coated with one or more of a laundry list of substances, do not guide the skilled artisan in arriving at Appellants' specific method for culturing **primary liver cells**, comprising providing a cell adhesion promoting surface including a CAR material, collagen I and poly-L-ornithine. Rather, the combined teachings of these two references in combination with the teachings of the '897 application, the '616 patent and the '436 patent merely invite experimentation, and, as discussed herein, an invitation to experiment is not sufficient grounds to reject an invention as obvious.

8. **Claims Appendix**

An appendix containing a copy of the claims involved in the appeal.

9. **Evidence Appendix**

None.

10. **Related Proceedings Appendix**

None.

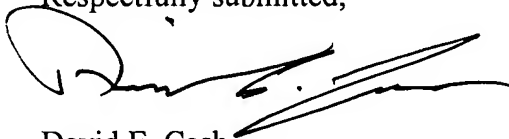
In re: Guarino *et al.*
Appl. No.: 10/664,037
Filing Date: September 17, 2003

CONCLUSION

Appellants maintain that the Examiner has failed to carry her burden of establishing that the claims are not patentable because she has (a) failed to prove that the claims are not novel and (b) failed to establish that the claims are obvious. Accordingly, claims 1-3, 6-8, 10, 12-16, 58, and 61-67 are allowable. For these reasons, presented in detail above, Appellants respectfully request that the rejections be overturned.

It is not believed that extensions of time are required. However, in the event that extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

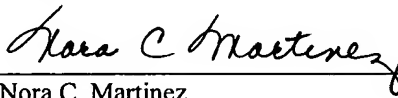


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Nora C. Martinez

CLAIMS APPENDIX

APPEALED CLAIMS

1. (Previously Presented) A method for culturing primary liver cells comprising:

(a) providing a polymer composition comprising a CAR material, and one or more ECM proteins and a polycationic polymer bound to said CAR material, wherein said CAR material, said one or more ECM proteins, and said polycationic polymer thereby form a cell adhesion promoting surface; and

(b) incubating said liver cells in the presence of said surface in a medium that supports growth and/or maintenance of said liver cells, such that said liver cells attach to said surface;
thereby culturing said liver cells.

2. (Previously Presented) The method of claim 1, wherein said one or more ECM proteins are selected from the group consisting of collagen I, collagen III, collagen IV, collagen VI, laminin, elastin, vitronectin, and fibronectin.

3. (Previously Presented) The method of claim 2, wherein said one or more ECM proteins are selected from the group consisting of elastin, collagen I, collagen IV, and collagen VI.

4-5. (Canceled)

6. (Previously Presented) The method of claim 1, wherein said polycationic polymer is selected from the group consisting of polyethyleneimine (PEI), poly-D-lysine (PDL), poly-L-lysine (PLL), poly-D-ornithine (PDO), and poly-L-ornithine (PLO).

7. (Previously Presented) The method of claim 1, wherein said one or more ECM proteins and said polycationic polymer are noncovalently bound to said CAR material.

8. (Previously Presented) The method of claim 1, wherein said one or more ECM proteins and said polycationic polymer are covalently bound to said CAR material.

9. (Withdrawn)

10. (Previously Presented) The method of claim 1, wherein said one or more ECM proteins is collagen I and said polycationic polymer is poly-L-ornithine.

11. (Withdrawn)

12. (Original) The method of claim 1, wherein said CAR material is selected from the group consisting of hyaluronic acid (HA), alginic acid (AA), polyethylene glycol (PEG), polyethylene oxide (PEO), and polyhydroxyethyl methacrylate (poly-HEMA).

13. (Original) The method of claim 12, wherein the CAR material is HA.

14. (Previously Presented) The method of claim 1, wherein said one or more ECM proteins are in the form of a 3-dimensional (3D) scaffold.

15 (Previously Presented) The method of claim 1, wherein said polymer composition is a flexible material.

16. (Original) The method of claim 15, wherein the flexible material is a polydimethyl siloxane (PDMS) or other silicone-based polymer.

17-57. (Canceled)

58. (Previously Presented) A method for culturing primary liver cells comprising:
(a) providing a polymer composition comprising a CAR material, and collagen I and poly-L-ornithine bound to said CAR material, wherein said CAR material, collagen I and poly-L-ornithine thereby form a cell adhesion promoting surface; and

(b) incubating said liver cells in the presence of said surface in a medium that supports growth and/or maintenance of said liver cells, such that said liver cells attach to said surface;
thereby culturing said liver cells.

59-60. (Withdrawn)

61. (Previously Presented) The method of claim 1, wherein the cells are rat primary liver cells or human primary liver cells.

62. (Previously Presented) The method of claim 1, wherein said liver cells are maintained in a functional state.

63. (Previously Presented) The method of claim 62, wherein said liver cells secrete albumin.

64. (Previously Presented) The method of claim 62, wherein said liver cells maintain cytochrome P-450 activity.

65. (Previously Presented) The method of claim 58, wherein said liver cells are maintained in a functional state.

66. (Previously Presented) The method of claim 65, wherein said liver cells secrete albumin.

67. (Previously Presented) The method of claim 65, wherein said liver cells maintain cytochrome P-450 activity.



EVIDENCE APPENDIX

NONE



RELATED PROCEEDINGS APPENDIX

NONE